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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/676,292	10/01/2003	Toshihiro Mitaka	1285-7 PCT/CON	7064

23869 7590 08/04/2005

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 08/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/676,292	MITAKA ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-34 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-34 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-34 are pending.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1 and 2, drawn to small hepatocyte-rich colonies, classified in class 435, subclass 370.

II. Claim 3, drawn to a process for preparing small hepatocyte-rich colonies comprising the step of dividing isolated hepatocytes into a heavy fraction enriched with parenchymal cells and a light fraction enriched with non-parenchymal cells, and recovering the light fraction, classified in class 435, subclass 370.

III. Claim 4, drawn to a process for preparing small hepatocyte-rich colonies comprising the step of dissociating colonies from a culture dish by reacting an enzyme or without reacting an enzyme on small hepatocytes forming the colonies to recover the small hepatocytes, classified in class 435, subclass 370.

IV. Claims 5 and 6, drawn to a process for maturating small hepatocyte-rich colonies into a liver tissue comprising the step of adding an extracellular matrix to the medium containing the cultured small hepatocyte-rich colonies, classified in class 435, subclass 370.

V. Claims 7-10, drawn to a process for maturating small hepatocyte-rich colonies into a liver tissue or preparing a liver tissue for transplantation, comprising the

step of placing small hepatocyte-rich colonies on a bioabsorbable sheet, classified in class 435, subclass 370.

VI. Claims 11, 15, 19, 21, 25, 27, 31, and 33, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 5, classified in class 435, subclass 6.

VII. Claims 12, 16, 20, 22, 26, 28, 32, and 34, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 7, classified in class 435, subclass 6.

VIII. Claims 13, 17, 23, and 29, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 5, wherein the induction or repression pattern of a gene is compared with an induction or repression pattern of the gene associated with a chemical substance having a known effect, classified in class 435, subclass 6.

IX. Claims 14, 18, 24, and 30, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 7, wherein the induction or repression pattern of a gene is compared with an induction or repression pattern of the gene associated with a chemical substance having a known effect, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for inventive groups that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: Groups II-XIII are directed to methods that are distinct both physically and functionally, and are not required one for the other. The groups serve different purposes: Groups II and III are processes for preparing small hepatocyte-rich colonies, Groups IV and V are processes for maturating small hepatocyte-rich colonies into a liver tissue, whereas Groups VI-IX are methods of estimating an effect of a chemical substance on a liver function *in vitro*. Furthermore, each of these sets of methods with different functions require different steps.

Though Groups II and III are both processes for preparing small hepatocyte-rich colonies, they both require different steps and components. Group II requires the step of dividing the isolated hepatocytes into a heavy fraction enriched with parenchymal cells and a light fraction enriched with non-parenchymal cells, which is not required by Group III. Additionally, Group III indicates that colonies from a culture dish may be dissociated by reacting an enzyme on small hepatocytes forming the colonies to recover the small hepatocytes, which is not required by Group II.

Similiarly, Groups IV and V serve the same purpose, but require different steps. Group IV requires adding an extracellular matrix to a medium containing the cultured small hepatocyte-rich colonies, whereas Group V requires placing the small hepatocyte-rich colonies on a bioabsorbable sheet.

With respect to Groups VI-IX, Groups VIII-IX require comparison of the induction or repression pattern of a gene with an induction or repression pattern of the gene associated with a chemical substance having a known effect, which is not required by Groups VI-VII. Groups VI and VIII differ from Groups VII and IX in that they use small hepatocyte-rich colonies matured according to the process of claim 5, as opposed to the same types of colonies obtainable by the process of claim 7.

Therefore, a search and examination of the above methods in one patent application would result in an undue burden, since the searches for the methods are not co-extensive, the classification is different, and the subject matter is divergent.

Inventions II and III are related to Invention I as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the product of Invention I may be made by materially different processes, including the processes of Invention II and III which, as discussed above, are patentably distinct.

Invention I is related to Inventions IV and V as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product, small hepatocyte-rich colonies,

may be used in materially different processes, such as in experimental procedures resulting in the induction of drug-metabolizing enzymes. Moreover, the processes of Inventions IV and V are patentably distinct, as discussed above.

The products of Inventions IV and V are related to Inventions VI-IX as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, Inventions IV and V can be used in materially different processes such as the distinct methods of Inventions VI-IX (see discussion above).

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter and different classification, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species of the claimed invention:

(a) the drug-metabolizing enzyme genes of claim 27;

(b) the drug-metabolizing enzyme genes of claim 28;

(c) the drug-metabolizing enzyme genes of claim 29;

(d) the drug-metabolizing enzyme genes of claim 30;

(e) the drug-metabolizing enzyme genes of claim 31;

(f) the drug-metabolizing enzyme genes of claim 32.

If applicant elects Group VI, as set forth above, applicant is further required under 35 U.S.C. 121 to elect a **single** disclosed species of from each of (a) and (e) set forth above, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 11 and 19 are generic.

If applicant elects Group VII, as set forth above, applicant is further required under 35 U.S.C. 121 to elect a **single** disclosed species of from each of (b) and (f) set forth above, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 12 and 20 are generic.

If applicant elects Group VIII, as set forth above, applicant is further required under 35 U.S.C. 121 to elect a **single** disclosed species of from (c) set forth above, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 13 is generic.

If applicant elects Group IX, as set forth above, applicant is further required under 35 U.S.C. 121 to elect a **single** disclosed species of from (d) set forth above, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 14 is generic.

Thus, a properly responsive election would appear as follows: --

Applicant hereby elects, with traverse, Group IX, claims 14, 18, 24, and 30, drawn to a method of estimating an effect of a chemical substance on a liver function *in vitro* using the small hepatocyte-rich colonies matured according to the process of claim 7, wherein the

induction or repression pattern of a gene is compared with an induction or repression pattern of the gene associated with a chemical substance having a known effect. Applicant also elects, with traverse, CYP2B1 as the drug-metabolizing enzyme gene of species (d).

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Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of M.P.E.P. § 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 C.F.R. 1.116; amendments submitted after allowance are governed by 37 C.F.R. 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 C.F.R. 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35U.S.C. §§101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper

restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to maintain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the protection against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See M.P.E.P. § 804.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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